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WO 01/40146 A1

(54) Title: PROCESS FOR PREPARING AMBIENT TEMPERATURE IONIC LIQUIDS

(57) Abstract: A process for preparing an ionic liquid or salt, preferably in which the cation comprises an N-alkylated base and the anion is a carboxylate, formed by reaction between an organic base and an alkylating agent, wherein the alkylating agent is a fluorinated ester or an alkyl sulfonate, is described. Suitable organic bases include imidazoles, substituted imidazoles, pyridines and substituted pyridines. The so-formed products can be subsequently transformed into different ionic liquids or salts by metathesis.

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10 "Process for Preparing Ambient Temperature Ionic
11 Liquids"

12

13 This invention relates to a process for processing
14 ambient temperature ionic liquids.

15

16 Ambient temperature ionic liquids based upon the 1,3-
17 dialkylimidazolium cation were first reported in 1982
18 by Wilkes *et al*¹. These systems were based upon the
19 chloroaluminate anion and although they possess many
20 useful properties (e.g. wide liquids, thermal stability
21 and large electrochemical window) they are reactive to
22 certain materials and are sensitive to moisture. An
23 air and water stable system was developed by Wilkes and
24 Zaworotko in 1992 based upon the tetrafluoroborate
25 anion². Since this report a wide range of ionic liquids
26 containing different anions have appeared in the
27 literature³. These systems have received much attention
28 and recent studies have shown that ambient temperature
29 ionic liquids can be used as solvents for a range of
30 chemical reactions including polymerisation⁴,

hydrogenation⁵, Friedel-Crafts acylations⁶ and for the Diels-Alder reaction⁷.

3

4 The principal route currently employed in the synthesis
5 of the air and moisture stable 1,3-dialkylimidazolium
6 ionic liquids is outlined in Scheme 1.

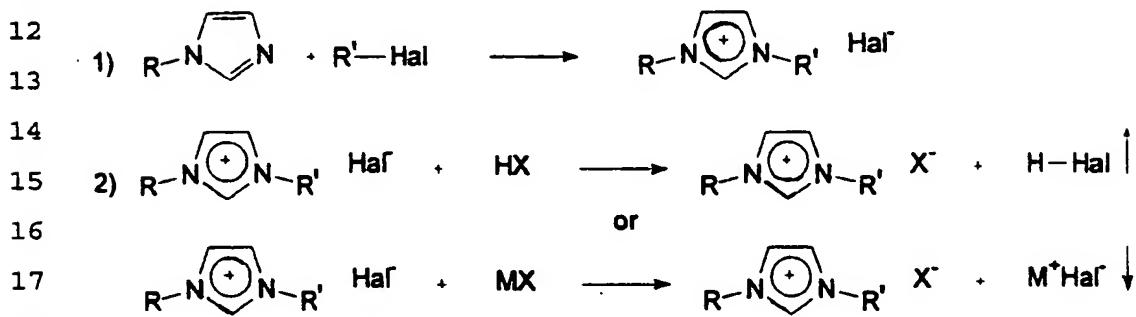
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23
24 The first step with this method is the alkylation of 1-
25 alkylimidazole with a haloalkane to give a 1,3-
26 dialkylimidazolium halide salt. The second step is
27 metathesis of the halide for the appropriate anion.
28 The second step can be carried out with either an acid
29 or a metal salt to eliminate H-Hal as or precipitate
30 M⁺Hal respectively. It is here that the intrinsically
31 good solvating properties of these ionic liquids become
32 a problem. In many of the syntheses the ionic liquids

1 solvate the halide waste so effectively that complete
2 removal is not effected. Halide contamination of the
3 ionic liquids is a problem that must be overcome for
4 them to be used as reaction solvents on a large scale.
5 For instance, when used as media for transition metal
6 catalysed reactions the presence of strongly co-
7 ordinating halide ions have been shown to reduce
8 catalyst activity⁵. The opportunity exists in many
9 reactions for the residual halides to be oxidised to
10 halogens which will result with many substrates and can
11 corrode apparatus. In addition, this method always
12 generates a stoicheiometric amount of halide salt as a
13 waste product. When metathesis is carried out using a
14 silver salt the route becomes prohibitively expensive
15 upon scale up. Employing the alkali metal salts
16 reduces the cost, but not the waste.

17

18 We have developed a new method for the synthesis of the
19 air- and moisture-stable ionic liquids that overcomes
20 the possibility of halide impurities and reduces the
21 amount of waste products. This method is based upon
22 the use of fluorinated esters or alkyl sulfonates as
23 replacements for haloalkanes.

24

25 Thus, according to one aspect of the present invention,
26 there is provided a process for preparing an ionic
27 liquid or salt formed by reaction between an organic
28 base and an alkylating agent, wherein the alkylating
29 agent is a fluorinated ester or an alkyl sulfonate.

30

31 The so-formed product of the organic base and ester or
32 sulfonate could subsequently be transformed into a

1 different ionic liquid or salt with a range of
2 different anions by metathesis, preferably using an
3 acid or metal salt.

4

5 In one embodiment of the present invention, the cation
6 formed is an N-alkylated base.

7

8 For this, the organic base could be an imidazole or a
9 substituted imidazole. Preferably, the substituted
10 imidazolium salt is a 1,3-dialkylimidazolium
11 trifluoroethanoate and the (n-1)-substituted imidazole
12 is a 1-alkylimidazole.

13

14 Alternatively, the organic base is a pyridine or a
15 substituted pyridine.

16

17 Other organic bases include the phosphines and
18 sulfides.

19

20 Also preferably a co-solvent is used.

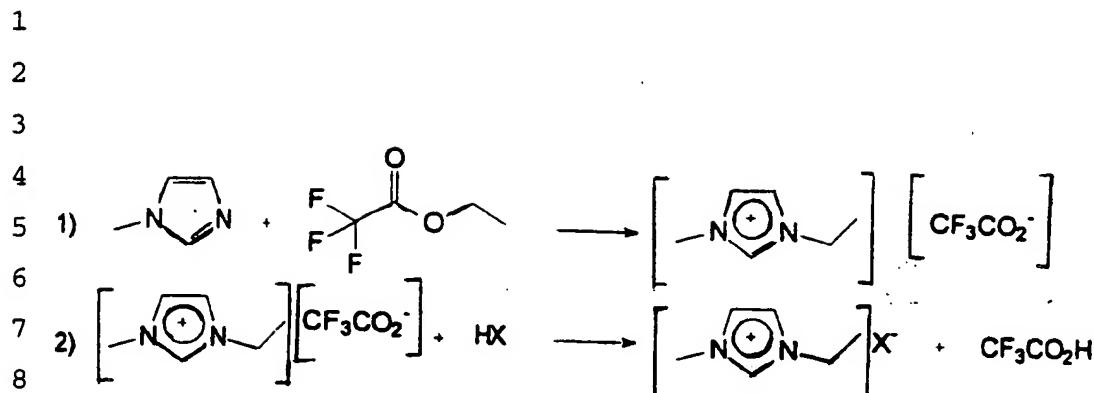
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22 The following description will focus on using the
23 organic base 1-methylimidazole, the imidazole most
24 commonly used in the preparation of ambient temperature
25 ionic liquids, and ethyl trifluoroethanoate as the
26 alkylating agent.

27

28 The synthesis is similar to that mentioned above in
29 Scheme 1, in that there is an alkylation and a
30 metathesis step to give the desired ionic liquid as
31 shown in Scheme 2.

32



10

11 Scheme 2.

12

13 The reaction of 1-methylimidazole with ethyl
 14 trifluoroethanoate to give 1-ethyl-3-methylimidazolium
 15 trifluoroethanoate, [emim][TFA], proceeds cleanly and
 16 smoothly at moderate temperature (70°C). However, some
 17 reduction in the rate of reaction may occur as the
 18 reaction proceeds. The primary reason for the
 19 reduction in rate is that unreacted 1-methylimidazole
 20 concentrates in the ionic liquid phase as it forms,
 21 while the ethyl trifluoroethanoate is only slightly
 22 soluble in [emim][TFA]; thus reactants are kept apart.
 23 Addition of a co-solvent to solubilise reactants and
 24 products, for example acetonitrile, overcomes this
 25 problem and a significant rate enhancement is observed.
 26 Alternatively, the reaction may be performed in an
 27 autoclave.

28

29 [emim][TFA] is an ambient temperature ionic liquid with
 30 all the expected characteristics in its own right. In
 31 addition, it is a good starting point for the synthesis

1 of other air- and moisture-stable ionic liquids with
2 metathesis of the trifluoroethanoate anion easily
3 achieved. Addition of the desired acid to [emim][TFA]
4 yields a reaction mixture with only one volatile
5 material, trifluoroethanoic acid (b.pt.72 °C), which is
6 easily removed under vacuum. This is true as long as
7 the added acid is of higher boiling point than CF₃CO₂H,
8 which most acids of interest are (e.g. HPF₆, HBF₄,
9 H₃PM₁₂O₄₀ (M = W, Mo), H₃PO₄). This gives the desired
10 ionic liquid, without extractions and washings, in a
11 halide free state.

12

13 The use of longer alkyl chain esters (e.g. hexyl
14 trifluoroethanoate) works equally as well with 1-
15 alkylimidazoles to give the desired product. The use
16 of more fluorinated esters (e.g. ethyl
17 heptafluorobutanoate) is still possible although they
18 may have the drawback of generating a less volatile
19 carboxylic acid by-product.

20

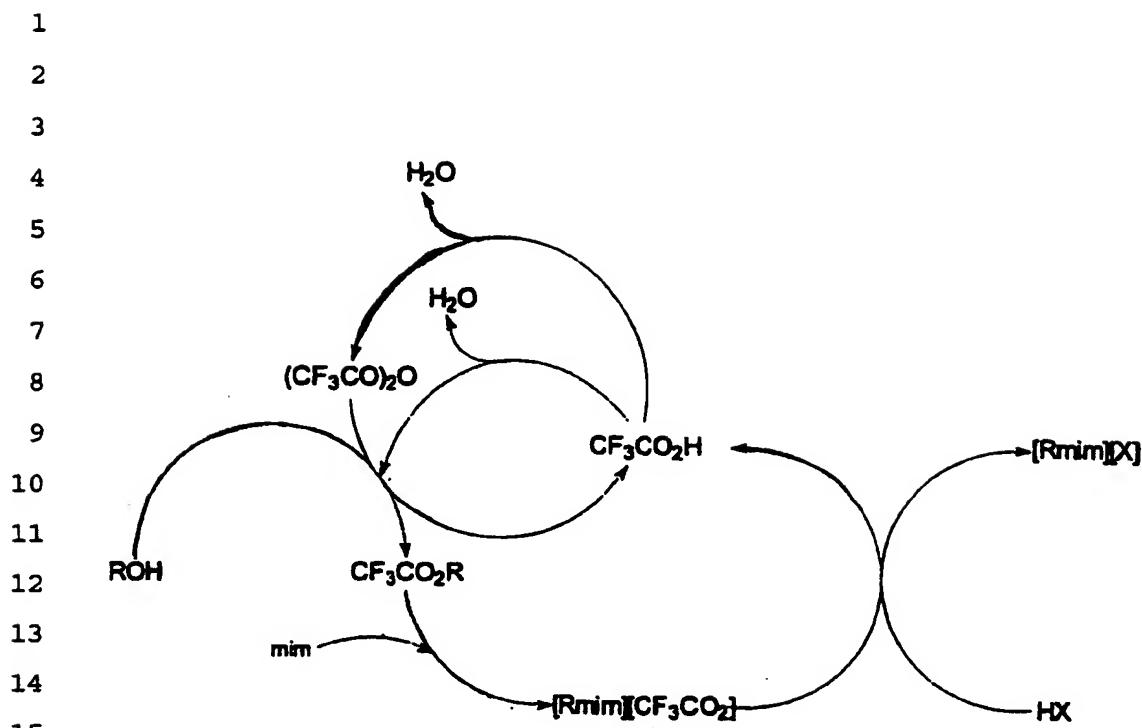
21 Alkyl sulfonates for use as the alkylating agent are
22 also well known in the art, such as a methyl sulfonate;
23 more particularly butyl methylsulfonate.

24

25 According to a second aspect of the present invention
26 there is provided a process for preparing an ionic
27 liquid or salt formed by reaction between an organic
28 base and fluorinated alkylating agent whenever the so-
29 formed fluorinated by-product has a lower boiling point
30 than the acid added to the alkylating agent.

31

1 The cation formed is preferably an N-alkylated base.
2 This is a general method that can be used to synthesise
3 a range of (imidazolium, possibly substituted
4 imidazolium) ionic liquids and low melting point salts.
5
6 The present invention extends to any product obtainable
7 from any of the new processes herein described.
8 Particularly, it extends to a 1,3-dialkylimidazolium-
9 based ionic liquid whenever prepared by reacting
10 1-alkylimidazole with a fluorinated ester, followed by
11 metathesis.
12
13 The present invention also extends to the use of any
14 ester able to act in a similar manner to form an
15 ambient temperature ionic liquid with an organic base.
16
17 The reaction conditions required to effect the
18 processes of the present invention will be known or
19 calculable to those skilled in the art.
20
21 The use of fluorinated compounds, although expensive,
22 is desired for two reasons. Firstly, fluorination of
23 the ester activates the molecule for the alkylation
24 step, and secondly, fluorinated products are more
25 volatile and of lower boiling point than their non-
26 fluorinated analogues, thus making separation of the
27 ionic liquid easier. The cost of using fluorinated
28 esters should not be prohibitively expensive as the
29 carboxylic acid by-product can be recycled. An overall
30 process is envisaged as shown in Scheme 3.



Scheme 3

19

20 R = hydrocarbyl, or substituted hydrocarbyl.

21 X = any anion such as nitrate, tetrafluoroborate,
22 hexafluorophosphate, etc.

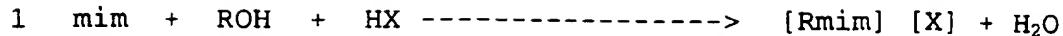
23 mim = 1-methylimidazole.

24

25 R and X are used in their normal context as is well
26 known in the art.

27

28 As scheme 3 shows, the waste trifluoroethanoic acid is
29 recovered and converted into the reactive ester either
30 through a straight esterification or via the anhydride.
31 This gives the following balanced equation for the
32 synthesis of ambient temperature ionic liquids;



2

3 The present invention thus provides a new synthetic
4 route to ambient temperature ionic liquids that ensures
5 the product is halide-free. If the metathesis is
6 performed with an acid rather than a metal salt, then
7 the product will be both halide-free and metal-free.
8 In addition, the alkylating agent can be regenerated
9 from inexpensive and readily available materials, thus
10 reducing waste.

11

12 **Experimental**

13

14 **Preparation of 1-ethyl-3-methylimidazolium**
15 **trifluoroethanoate, [emim][TFA].**

16

17 1-Methylimidazole (2.5g, 30.4mmol) and ethyl
18 trifluoroethanoate (25.8g, 181.6mmol) were dissolved in
19 ethanenitrile (20cm³). The resultant solution was
20 placed in a sealed glass vessel and stirred at 70°C for
21 5 days giving a pale yellow solution. The volatiles
22 were removed *in vacuo* giving [emim][TFA] in 100% yield.

23

24 **Preparation of 1-ethyl-3-methylimidazolium**
25 **tetrafluoroborate, [emim][BF₄]**

26

27 To [emim][TFA] (1.0g, 4.5mmol) was added one equivalent
28 of fluoroboric acid (0.412cm³ of 10.8M aq. solution, 4.5
29 mmol) and the mixture was stirred overnight at room
30 temperature. Heating under vacuum at 100°C removes
31 trifluoroethanoic acid and water giving [emim][BF₄].

1 **Preparation of 1-ethyl-3-methylimidazolium
2 hexafluorophosphate, [emim][PF₆]**

3

4 To [emim][TFA] (2.0g, 8.9mmol) dissolved in water
5 (10cm³) was added hexafluorophosphoric acid (2cm³ of
6 6.79M aq. solution, 13.58mmol). This gave [emim][PF₆]
7 as a white precipitate which was collected by vacuum
8 filtration.

9

10 **Preparation of butyl methanesulfonate (BuOMs)**

11

12 To a 500 cm³ round-bottomed flask, equipped with a
13 magnetic stirrer and pressure equalising dropping
14 funnel, was added butanol (55.6 g, 0.75 mol),
15 triethylamine (55.7 g, 0.55 mol) and dichloromethane
16 (300 cm³). Methanesulfonyl chloride (57.3 g, 0.05 mol)
17 was then added dropwise over a two-hour period from the
18 dropping funnel, with cooling from an ice bath. The
19 mixture was stirred for a further 24 hours at room
20 temperature. The reaction mixture was filtered,
21 concentrated on a rotary evaporator, and distilled (bp
22 - 80-90 °C at 5 mm Hg). This gave 68.1 g (98%) of a
23 colourless oil.

24

25 **Preparation of 1-butyl-3-methylimidazolium
26 methanesulfonate ([bmim][Oms])**

27

28 In a 100 cm³ round-bottomed flask, was added butyl
29 methanesulfonate (15.3 g, 0.10 mol) and
30 1-methylimidazole (8.21g, 0.10mol). A reflux condenser
31 was attached and the mixture heated at 100 °C for 48

1 hours. A vacuum was applied to the flask (1 mm Hg) to
2 remove unreacted starting materials for 12 hours at
3 80 °C. The low-melting salt [bmim][Oms] (22.3 g, 95%)
4 solidified on cooling.

5

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1 CLAIMS

2

3 1. A process for preparing an ionic liquid or salt
4 formed by reaction between an organic base and an
5 alkylating agent, wherein the alkylating agent is a
6 fluorinated ester or an alkyl sulfonate.

7

8 2. A process as claimed in Claim 1 wherein the cation
9 formed is an N-alkylated base.

10

11 3. A process as claimed in Claim 2 wherein the organic
12 base is an imidazole or a substituted imidazole.

13

14 4. A process as claimed in Claim 3 wherein the organic
15 base is a 1-alkylimidazole.

16

17 5. A process as claimed in Claim 4 wherein the organic
18 base is 1-methylimidazole.

19

20 6. A process as claimed in Claim 2 wherein the organic
21 base is a pyridine or a substituted pyridine.

22

23 7. A process as claimed in Claim 6 wherein the organic
24 base is an alkylpyridine.

25

26 8. A process as claimed in Claim 1 wherein the organic
27 base is a phosphine or a sulphide

28

29 9. A process as claimed in any one of the preceding
30 Claims wherein a co-solvent is used.

31

32 10. A process as claimed in Claim 9 wherein the co-
33 solvent is acetonitrile.

1

2 11. A process as claimed in any one of the preceding
3 Claims wherein the reaction is carried out under
4 pressure.

5

6 12. A process as claimed in any one of the preceding
7 Claims wherein the anion formed is
8 trifluoroethanoate.

9

10 13. A process as claimed in any one of the preceding
11 Claims wherein the alkylating agent is ethyl
12 trifluoroethanoate.

13

14 14. A process as claimed in any one of Claims 1-12
15 wherein the alkylating agent is a methyl sulfonate.

16

17 15. A process as claimed in Claim 14 wherein the
18 alkylating agent is butyl methylsulfonate.

19

20 16. A process as claimed in any one of the preceding
21 Claims wherein the so-formed product is subsequently
22 transformed into a different ionic liquid or salt by
23 metathesis.

24

25 17. A process as claimed in Claim 16 wherein an acid or
26 metal salt is used for the metathesis.

27

28 18. A process for preparing an ionic liquid or salt
29 formed by reaction between an organic base and
30 fluorinated alkylating agent whenever the so-formed
31 fluorinated by-product has a lower boiling point
32 than the acid added to the alkylating agent.

33

1 19. An ionic liquid or salt whenever prepared by a
2 process as claimed in Claims 1-18.

3

4 20. A 1, 3-dialkylimidazolium trifluoroethanoate
5 whenever prepared by a process as claimed in any one
6 of Claims 1-18.

7

8

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/GB 00/04584

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07B37/02 B01J31/02 B01J37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C07B B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 21871 A (BP CHEM INT LTD ;ABDUL SADA ALA A K (GB); AMBLER PHILIP WILLIAM (G) 17 August 1995 (1995-08-17) cited in the application the whole document ----- X	1
X	BEILSTEIN INFORMATION SERVICE; FILE: XFIRE, XP002163372 see BRN: 7736754 & HOWARTH ET AL.: TETRAHEDRON LETT., vol. 38, no. 17, 1997, pages 3097-3100, -----	20

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/04584

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